SENSORY INFORMATION FROM AFFERENT NEURONS

Contract No.: NIH-NINDS-NO1-NS-6-2339

FINAL REPORT

For the period

31 March 1996 to 30 March 2000

Prepared by

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Date of submission: 20 October 2000

I. Overall objectives of this research

Our aim was to develop and perfect, in an animal model, methods for chronic recording and processing of afferent activity produced by sensory receptors that could yield information about human fingertip contact, grasped object slip, finger position, and grasp force applicable for restoration of motor functions in the paralyzed human hand. The specified contract objectives were as follows:

1. Select recording methods that:
   a. Have the potential of providing safe, reliable recordings in humans for periods of years.
   b. When used in human applications, could provide relatively isolated information from the sensory endings in the thumb pad and in the finger pads of the second and third fingers.
   c. Could, in human applications, provide information from the proprioceptive receptors in the muscles of the hand and wrist.

2. Select an animal model suitable for chronic recording of afferent nerve activity, and give consideration to modeling electrode placement sites for a potential human neural prosthesis application.

3. Fabricate or obtain chronic electrodes and associated cables and percutaneous connectors for chronic recording of sensory afferent activity.
   a. Design electrodes and cables using biocompatible materials that would be suitable for potential future human implants.
   b. Design electrodes and cables with the goal of producing a chronic implant that causes minimal nerve damage.

4. Investigate the possibility of extracting information about contact, grasped object slip, limb position and contact force from chronically recorded neural activity using the animal model and electrodes from parts 2 and 3.
   a. Devise recording, processing, and detection methods to extract this information from recorded neural activity in a restrained animal.
   b. Modify these methods as needed to function in an unrestrained animal and in the presence of stimulation artifacts associated with functional electrical stimulation.
   c. Record activity for periods of at least 6 months and devise functional measures to track any change in neural response over this time.
   d. Evaluate any histological changes in the nerves that occurred over the period of chronic recording and, if possible, correlate these changes to changes in functional response.

5. Cooperate with other investigators in the Neural Prosthesis Program by collaboration and sharing of experimental findings.

II. Objectives that were achieved

1a. We evaluated the potential of providing safe, reliable recordings in humans for periods of years for two recording methods: multi-channel, multi-chambered nerve cuff electrodes (MCCs) or longitudinal intrafascicular electrodes (LIFEs), that were evaluated in two parallel series of animal implants. We found that using MCCs, the amplitude of recorded signals could diminish somewhat after a few weeks, but the cuffed nerves and electrodes generally remained stable for the duration of the experiments (6-12 months). By contrast, using LIFEs the amplitude of recorded nerve signals always diminished markedly during the first month after implant and continued to diminish over the following 5-8 months. MCCs such as those we used in these experiments can be expected to provide safe, reliable recordings in humans for periods of years, whereas LIFEs (at least of the design used in these experiments) would not be a reliable method for long-term recordings in humans.

1b. When used in human applications, both MCCs and LIFEs could be expected to provide relatively isolated information from the sensory endings in the thumb pad and in the finger pads of the second and third fingers, based on our results using an animal model in which MCCs or LIFEs were placed on median, ulnar and radial nerve trunks.

1c. When used in human applications, both MCCs and LIFEs could be expected to provide information from the proprioceptive receptors in the muscles of the hand and wrist, based on our results using an animal model in which MCCs or LIFEs were placed on median, ulnar and radial nerve trunks.

2. We selected the cat as an animal model suitable for chronic recording of afferent nerve activity, and chose the main peripheral nerve trunks in the cat forelimb or the cat hindlimb to give consideration to modeling electrode placement sites for potential human neural prosthesis applications.

3. We fabricated or obtained from two collaborators custom-designed chronic MCC and LIFE electrodes and associated cables and percutaneous connectors for chronic recording of sensory afferent activity. As a result of this research, we have converged on reliable new designs of nerve cuffs, a cuff closing system, multi-chambered cuff designs, and laser–based methods of nerve cuff fabrication amenable to serial production for commercial use in human patients. One US patent was awarded and additional patents were filed on these inventions.

3a. We designed MCC or LIFE electrodes and cables using stainless steel or Pt-Ir wire, Teflon insulation, silicone elastomers and monofilament nylon sutures, all biocompatible materials that would be suitable for potential future human implants.

3b. We chose the nerve implant sites and designed the electrodes and cables with the goal of producing a chronic implant that caused minimal nerve damage.

4. In experiments performed in chronically implanted animals under general anesthesia, using the animal model and electrodes from parts 2 and 3, we investigated the possibility of

extracting information about contact, grasped object slip, limb position and contact force from chronically recorded neural activity.

4a. We devised recording, processing, and detection methods to extract information about contact, grasped object slip, limb position and contact force from recorded neural activity in a restrained animal under general anesthesia.

4b. For single-channel cuff recordings, we were able to modify these methods as needed to function in an unrestrained animal and in the presence of stimulation artifacts associated with functional electrical stimulation.

4c. We recorded activity for periods of at least 6 months and devised functional measures, based on amplitude and latency of nerve compound action potentials (CAPs) evoked with electrical nerve stimulation, to track any change in neural response over this time. It is important to emphasize that the implanted animals were not restricted or caged, but on the contrary they were group-housed in a medium-sized room equipped with steps of different heights, up to 2 m, and were allowed to range freely at all times except immediately after surgery or anesthesia, when they were kept isolated for a day or two until fully recovered. The implanted animals typically jumped up and down steps and counters, and climbed up and down a wire fence, generally with no noticeable sign of motor deficit in the case of implanted MCCs or LIFEs, and with no noticeable deficit in nerve CAP amplitudes or nerve morphology in the case of implanted MCCs aside from the observations listed in item 1a, above.

III. Objectives that were not achieved

4b. For multi-channel nerve recordings, we were not able, in the time available, to fully modify these methods as needed to function in an unrestrained animal and in the presence of stimulation artifacts associated with functional electrical stimulation, although we were able to complete a similar project that involved recording from several single-channel nerve cuffs. We see no intrinsic reason why this objective could not be achieved in the future, given sufficient time and resources.

4d. In the time available, we were not able to evaluate the histological changes in the nerves that occurred over the period of chronic recording with multi-channel electrodes. However, we were able to recover nerve samples from the last five animals implanted with multi-chambered cuffs and we processed these histologically for electronmicroscopic examination. We are currently continuing with quantitative morphometric analysis, and intend to complete this study using other funding.

IV. Recommendations for future research & development

The degree of recording selectivity achievable for a wider variety of applications and the practical limitations to using multi-chambered nerve cuffs for multi-channel nerve recording

as well as for multi-channel nerve stimulation should be studied in greater detail in future work.

V. Publications supported by this Contract

Refereed Journal Articles

1. Strange, K. and Hoffer, J.A. Gait phase information provided by sensory nerve activity during walking: applicability as state controller feedback for FES. **IEEE Trans. Biomed. Engineering 46:**797-809, 1999.

2. Strange, K. and Hoffer, J.A. Restoration of use of paralyzed limb muscles using sensory nerve signals for state control of FES-assisted walking. **IEEE Trans. Rehab. Engineering 7:**289-300, 1999.

3. Hoffer, J.A. and K. Kallesøe, Nerve cuffs for nerve repair and regeneration. **Progr. Brain Res**. **128:**121-134, 2000.

Invited Reviews

4. Hoffer, J.A., Stein, R.B., Haugland, M., Sinkjær, T., Durfee, W.K., Schwartz, A.B., Loeb, G.E. and Kantor, C. Neural signals for command control and feedback in functional neuromuscular stimulation: a review. **J. Rehab. Res. & Dev. 33**:145-157, 1996.

5. Hoffer, J.A. and K. Kallesøe, How to use nerve cuffs to stimulate, record or modulate neural activity. Chapter 5 in **Neural Prostheses for Restoration of Sensory and Motor Function**, K.A. Moxon and J.K. Chapin, Eds. CRC Press, pp. 139-175, 2000.

Conference Proceedings

6. Hoffer, J.A., K.D. Strange, P.R. Christensen, Y. Chen and K.Yoshida. Multichannel recordings from peripheral nerves: 1. Properties of multi-contact cuff (MCC) and longitudinal intra-fascicular electrode (LIFE) arrays implanted in cat forelimb nerves. **IFESS/Neural Prostheses V Int'l. Conf**., Vancouver, BC, pp. 239-240, 1997.

7. Chen, Y., P.R. Christensen, K.D. Strange and J.A. Hoffer. Multichannel recordings from peripheral nerves: 2. Measurement of selectivity. **IFESS/Neural Prostheses V Int'l. Conf**., Vancouver, BC, pp. 241-242, 1997.

8. Strange, K.D., P.R. Christensen, Y. Chen, K. Yoshida and J.A. Hoffer. Multichannel recordings from peripheral nerves: 3. Evaluation of selectivity using electrical stimulation of individual digits. **IFESS/Neural Prostheses V Int'l. Conf**., Vancouver, BC, pp. 243-244, 1997.

9. Christensen, P.R., Y. Chen, K. D. Strange and J. A. Hoffer. Multichannel recordings from peripheral nerves: 4. Evaluation of selectivity using mechanical stimulation of individual digits. **IFESS/Neural Prostheses V Int'l. Conf**., Vancouver, BC, pp. 217-218, 1997.

10. Crouch, D., K.D. Strange and J.A. Hoffer. Morphometric analysis of cat median nerves after long-term implantation of nerve cuff recording electrodes. **IFESS/Neural Prostheses V Int'l. Conf**., Vancouver, BC, pp. 245-246, 1997.

11. Hansen, M., J.A. Hoffer, K.D. Strange and Y. Chen. Sensory feedback for control of reaching and grasping using functional electrical stimulation. **IFESS/Neural Prostheses V Int'l. Conf**., Vancouver, BC, pp. 253-254, 1997.

12. Kostov, A., B. Fuhr, K. Strange, and J. A. Hoffer, Potential role of afferent recordings as a sensory feedback in movement control systems: animal model. **Proc. IEEE - EMBS '98 Conference**, Hong Kong, pp. 2536-2539, Oct. 1998.

13. Hoffer, J.A. and K. Kallesøe, Nerve cuff electrodes for prosthetic and research applications, **IFESS '99,** Proc. 4th Annual Conf. Int. Functional Electrical Stimulation Soc., Sendai, Japan, pp. 113-116, Aug. 1999.

Patents Awarded

1. *Nerve Cuff having One or More Isolated Chambers:* United States Patent No. 5,824,027, awarded to J.A. Hoffer, Y. Chen, K. Strange and P. Christensen, October 20, 1998.

Patents Pending

Five additional patents were submitted in USA and/or Canada, Europe and Japan and are currently at various stages of review.

Published Abstracts

1. Kostov, A., Strange K., Stein, R.B., and Hoffer J.A. Adaptive Logic Networks in EMG-prediction from sensory nerve signals recorded in the cat's forelimb during walking. **Physiology Canada 26**: 104, 1996.

2. Hoffer, J.A., Y. Chen, P.R. Christensen and K.D. Strange. Sensory source identification with multi-contact nerve cuff electrodes. **Soc. Neurosci. Abstr. 23**: 612.17, 1997.

3. Hoffer, J.A. and Kallesøe, K. Stimulation, recording and modulation of nerve activity using implanted cuffs. **8th Intl. Symp. on Neural Regeneration**, Asilomar, CA, USA, Dec. 1999.

Theses related to this Project

1997 M.A.Sc. P. Christensen *Sensory source identification from nerve recordings with multi-channel electrode arrays*. Simon Fraser University.

1997 M.Sc. D. Crouch *Morphometric analysis of neural tissue following the long-term implantation of nerve cuffs in the cat forelimb.* Simon Fraser University.

1998 Ph.D. K. Kallesøe *Implantable transducers for neurokinesiological research and neural prostheses.* Simon Fraser University.

VI. Summary of work performed during Contract period

Year One

- Developed multi-chambered, multi-contact cuffs (MCCs) for implantation in upper limb of cats.
- Developed longitudinal intrafascicular electrodes (LIFEs) for implantation in upper limb of cats.
- Developed an apparatus and method for testing the selectivity of sensory signal detection during mechanical stimulation of digits in the cat's forepaw.
- Developed a method for testing the selectivity of sensory signal recording during electrical stimulation of digits in the cat's forepaw.
- Developed a method for extraction of sensory signals with machine learning techniques.
- Developed a Selectivity Index (SI) for multichannel sensory signal recordings.
- Performed acute experiments in three cats to test the SI method.
- Developed a methodology for testing the long-term stability of nerve compound action potentials (CAPs) upon stimulation of peripheral nerves.
- Trained six cats to perform walking tasks on a treadmill.
- Trained six cats to perform manipulation tasks with a forelimb.
- Implanted three cats with MCCs in the nerve trunks of one upper forelimb and EMG electrodes on 6-7 forelimb muscles (NIH 18, 19, 21).

- Implanted three cats with LIFEs in the nerve trunks of one upper forelimb and EMG electrodes on 6-7 forelimb muscles (NIH 20, 22, 23).
- Carried out multi-channel recordings from the six implanted cats at periodic intervals.

Year Two

- Completed multi-channel recordings from the six implanted cats for periods of 7-12 months.
- Tested the selectivity to mechanical inputs on individual digits of the forepaw in four cats.
- Tested the selectivity to electrical inputs on individual digits of the forepaw in the six cats.
- Recorded 2D forces, EMGs and multi-channel sensory nerve activity patterns during voluntary manipulation of a 2D joystick with the forepaw by awake cats.
- Completed the quantitative morphological analysis of four median nerves after tripolar nerve cuff implants over periods of 6-12 months.
- Implanted a second series of three cats with MCCs in the nerve trunks of one upper forelimb and EMG electrodes on 6-7 forelimb muscles (NIH 25,26,28).
- Implanted a second series of two cats with LIFEs in the nerve trunks of one upper forelimb and EMG electrodes on 6-7 forelimb muscles (NIH 24,27).
- Carried out multi-channel recordings from the five implanted cats at periodic intervals.

Year Three/Four

- Completed multi-channel recordings for 6 months from the five implanted cats (NIH 24-28).
- Investigated sensory receptive field selectivity of MCCs and LIFEs in response to controlled cutaneous and proprioceptive inputs to upper limb regions.
- Determined the reasons for premature mechanical failure of MCC leads in the latter series.
- Developed a hindlimb preparation to test multichannel nerve trunk recording and stimulation.
- Re-designed the MCC cuffs and re-engineered the cuff fabrication method.
- Implanted a third series of 7 cats with multichannel MCCs on the sciatic nerve and EMG electrodes on 6-7 calf muscles of one hindlimb (NIH 29-35).
- Documented the long-term stability of electrodes and nerves in five cats (NIH 30, 32-35) for periods of 6-12 months.

- Removed nerve samples from (NIH 30, 32-35) and processed histologically for electron-microscopic morphological examination and quantitative analysis.